

Examiner has not yet responded. Appropriate consideration of this matter is requested, for the second time.

Furthermore, claim 15 was cancelled by the previous amendment, so Applicants do not understand why this rejection has been maintained with respect to that claim. Appropriate consideration of the pending claims is respectfully requested.

Independent method claims 1 and 13 are directed to methods for producing sustained-release preparations. Applicants do not believe that these methods are anticipated by the cited reference.

A Declaration which should serve to aid the Examiner's understanding of Applicants' invention as set forth in the pending claims accompanies this response. This Declaration is very similar to the previously provided Declaration, but also contains additional detail, photos and Schemes to make the Applicants' arguments very clear.

The Examiner has expressed confusion over the "microcapsule powder" described in the comparative Examples. To clarify, Applicants would like to direct the Examiner's attention to page 1, lines 12-19 of the specification. The terms "microsphere" and "microcapsule" are used interchangeably (as indicated therein); and "microcapsule powder" is also explained.

In the Declaration, the preparation of microcapsule powder has been detailed in sections A1 and A2. The procedures for making the microcapsule powder would be well understood by those skilled in the art, especially given the definition which appears right on page 1 of the specification.

In addition, Flow Charts A1 and A2 provide a visual summary of the procedures of Examples A1 and A2 respectively.

Comparative Examples B1, B2 and B3 study the effects of using the microcapsule powder (generated in A1 or A2) in the presently claimed methods.

In B1, mannitol (not microcapsular) was subjected to the methods for producing a sustained-release preparation according to independent method claims 1 and 13. B1 corresponds to Experimental Example 1 of the previously provided Declaration. This example is representative of the method of the cited art. The preparation is also shown in the attached Pictures. Figures 1-4 show the preparation process, and Figures 5-9 show the undesirable result achieved after lyophilization. The result of not using a microcapsule was that undesirable scattering occurred.

In B3, a microcapsule including the active ingredient of leuporelin acetate was subjected to the methods for producing a sustained-release preparation according to independent U.S. Patent Application Serial No.: 09/600,744

method claims 1 and 13. B3 corresponds to Experimental Example 2 of the previously provided Declaration. The preparation is also shown in the attached Pictures. Figures 1-4 show the preparation process, and Figures 5-9 show the desirable result achieved after lyophilization. The result of using a microcapsule was that no undesirable scattering occurred.

In B2, a microcapsule without active ingredient was subjected to the methods for producing a sustained-release preparation according to independent method claims 1 and 13. The preparation is also shown in the attached Pictures. Figures 1-4 show the preparation process, and Figures 5-9 show the result achieved after lyophilization. The result of using a microcapsule (even without any active ingredient) was that no undesirable scattering occurred. Experiment B2 illustrates the point that the method is useful regardless of active ingredient.

The overall procedure of the presently claimed methods is also visually illustrated by Scheme 1.

These detailed pictures and Schemes have been provided to show the Examiner that their methods do not depend upon the use of certain materials. They have also been provided to prove that the pending claims are not broader in scope than the information provided in the supporting Declaration. Applicants believe that these submissions and their explanation should satisfy the Examiner.

Furthermore, Applicants note the Examiner's recommendation for "discussion of how the scattering is observed, and a statistical analysis of this data to demonstrate if the differences are significant". Applicants believe that this statement indicates a lack of understanding of Applicants' results. The scattering is not quantifiable, like light scattering. The scattering either occurs or does not occur. In Examples 7 and 8 of the specification, lack of scattering is stated as "Crumbling of the cake of the freeze-dried MCs, and also dispersing and scattering of the MCs out of the tray were not observed." in lines 7-9 and 30-32 of page 37. Because these phenomena did not occur, the methods presently claimed are highly useful for preparing medicines efficiently. Applicants assert that those skilled in the art, having knowledge and understanding of the process of lyophilization, and taking into account the experimental results explained in the specification, would have understood the scattering/lack of scattering described in the previously submitted Declaration. Since the Examiner apparently does not share this understanding, pictures have been provided to show scattering, in Figures 6-9. Statistical analysis of the phenomenon is inappropriate.

Therefore, Applicants stress that their invention as set forth in independent claims 1 and 13 (exemplified by B2 and B3) is not anticipated by the cited reference (exemplified and proven

U.S. Patent Application Serial No.: 09/600,744

by comparative example B1). The accompanying Declaration, photos and Schemes very plainly point this fact out, for the Examiner's edification. The Declaration, photos and Schemes should also convince the Examiner that the present claims are already commensurate in scope with the comparative tests.

Claims 3-5 and 8 depend upon claim 1. Applicants submit that these more specific dependent claims are also not anticipated by the cited reference for the reason provided above.

Therefore, Applicants respectfully request withdrawal of the Sec. 102 (b) rejection.

II. Discussion of the Rejection under 35 U.S.C. Sec. 103(a)

Claims 1-6, 8, 10, 13, 14, 16 and 18-22 stand rejected under 35 U.S.C. Sec. 103(a) as being unpatentable over Ueda *et al.* (EP 0 394 050 A2).

Applicants submit that their invention, as set forth in independent claims 1 and 13 as amended is not obvious over the cited reference. Applicants hereby incorporate their argument made in Section II above, which they believe to be equally applicable and convincing with respect to the obviousness rejection.

Claims 3-6 and 8 depend upon claim 1. Applicants submit that these more specific dependent claims are also not obvious in light of the cited reference for the reason provided above.

Independent claims 2, 14 and 20 specify a coating of a water-repelling base material for the inner face of a freeze-drying container, which is not disclosed in the cited art, as the Examiner has already recognized. Furthermore, Applicants do not believe that the limitation in their method claims for a water-repelling base material coating on the inner face of the freeze-drying container of the present invention is taught or suggested by the cited art.

Claims 3-6, 8 and 10 depend upon claim 2, claims 16, 18 and 19 depend upon claim 14 and claims 21 and 22 depend upon claim 20. Applicants submit that these more specific dependent claims are also not rendered obvious by the cited reference for the reason provided above.

Therefore, Applicants respectfully request withdrawal of the Sec. 103(a) rejection.

III. Conclusion

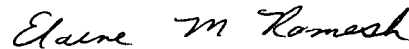
Reconsideration of the claims and allowance is requested. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

Dated: March 12, 2003

(847) 383-3391

(847) 383-3372



Elaine M. Ramesh, Ph.D., Reg. No. 43,032

Mark Chao, Ph.D., Reg. No. 37,293

Attorney for Applicants

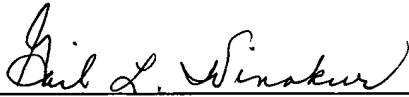
Customer No. 23,115

Takeda Pharmaceuticals North America, Inc.
Intellectual Property Department
Suite 500, 475 Half Day Road
Lincolnshire, IL 60069 USA

Certificate of Mailing under 37 CFR 1.10

The undersigned hereby certifies that this document, along with any attachments, is being deposited in an envelope addressed to The Commissioner of Patents and Trademarks, with sufficient postage with the United States Postal Service EXPRESS MAIL Post Office to Addressee Service on this date March 12, 2003.

Express Mail Label No. EV 193976425 US



Printed Name: Gail L. Winokur